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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,079	06/20/2001	Stefan Leo Jozef Masure	JAB-1458	7899

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EXAMINER	
PRIEBE, SCOTT DAVID	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 05/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,079	MASURE ET AL.	
	Examiner	Art Unit	
	Scott D. Priebe, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/28/05, 3/28/05, and 5/5/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,16-21,23-27,30-35 and 38-43* is/are pending in the application.

4a) Of the above claim(s) *5-8,19-21,23-27,30-35,38,39 and 41-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9-12,16-18 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 June 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20020226*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

As indicated below, the substitute specification filed 6/20/01 has not been entered. Consequently, the preliminary amendments of 10/03/03 and 6/30/04 have not been entered since these refer to the page and line numbers in the substitute specification. The substitute paper copy of the Sequence Listing filed 6/30/04 has been entered. The amendment filed 10/03/03 (page 5) refers to a replacement sheet for Figure 1. No such replacement sheet is present in the file.

The amendment filed 3/28/05 has been entered. The Office action of 4/13/05 was in error, since the amendment of 3/28/05 contained an S-signature, as pointed out in Applicant's Reply of 5/5/05.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-4, 9-12, 16-18, and 40 in the reply filed on 2/28/05 is acknowledged.

Claims 5-8, 19-21, 23-27, 30-35, 38, 39, and 41-43, in their entirety, and claims 17-18 as directed to tissue or a multicellular organism are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/28/05.

Information Disclosure Statement

The information disclosure statement filed 2/26/02 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent

literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein, as references 12 (Coffer), 22 (Dudek), and 49 (Philpott), has not been considered. No copies of these references have been provided.

Drawings

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because Fig. 2 is of poor quality and difficult to read due to the shading used. As indicated below, the substitute specification has not been entered, so the drawings referred to here are the drawings filed with the international application.

Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Specification

The substitute specification, including the substitute drawings, filed 6/20/01 has not been entered because it does not conform to 37 CFR 1.125(b) and (c) because: 1) the statement as to a lack of new matter under 37 CFR 1.125(b) is missing; and 2) a marked-up copy of the substitute specification has not been supplied (in addition to the clean copy). It is noted that in the substitute drawings, Fig. 4 omits panel B of original Figure 5. No explanation for this omission is provided. Original Fig. 1 was also omitted, presumably favor of just presenting SEQ ID NOs: 1

and 3. However, as indicated below, SEQ ID NO: 2 does not match the description of SEQ ID NO: 2 in the original specification as being nucleotides 11-1447 of the nucleotide sequence of original Fig. 1 (SEQ ID NO: 1).

All references to the specification below refer to the specification and drawings filed in the international application.

The substitute abstract has been entered.

The disclosure is objected to because of the following informalities:

SEQ ID NO: 2, as it appears in the Sequence Listing, appears to be incorrect. According to the specification on page 37, SEQ ID NO: 2 corresponds to nucleotides 11-1447 shown in Fig. 1, i.e. nucleotides 11-1447 of SEQ ID NO: 1. However, nucleotide 1440 of both Fig. 1 and SEQ ID NO: 1 is "G," whereas the corresponding nucleotide 1430 of SEQ ID NO: 2 is "A." Consequently, nucleotides 1429-1431 of SEQ ID NO: 2 (GAA) would encode Glu (or E) at amino acid 477 of the AKT-3 protein encoded thereby. In contrast, amino acid 477 of both SEQ ID NO: 3 and the amino acid sequence of Fig. 1 have Gly (or G) at this position, encoded by a "GGA" codon in SEQ ID NO: 1 and in the nucleotide sequence of Fig. 1. This appears to be an error in transcribing SEQ ID NO: 2. Nucleotide 1430 of SEQ ID NO: 2 should be --G-- instead of "A".

Also, nucleotide 1447 of SEQ ID NO: 1 and Fig. 1 does not have a corresponding nucleotide in SEQ ID NO: 2. The last nucleotide of SEQ ID NO: 2, nucleotide 1436, corresponds to nucleotide 1446 of SEQ ID NO: 1 and the nucleotide sequence of Fig. 1. As a result, the GAA codon encoding the C-terminal amino acid of SEQ ID NO: 3 and the amino acid sequence of Fig.

1 (Glu or E), is incomplete in SEQ ID NO: 2. Only two nucleotides of this codon (GA) are present in SEQ ID NO: 2. An --A-- nucleotide should be added at the 3' end of SEQ ID NO: 2 as nucleotide 1437, which would then correspond to nucleotide 1447 of SEQ ID NO: 1 and Fig. 1 as indicated in page 37 of the specification.

Appropriate correction is required. Such correction will require the submission of substitute computer readable form (CRF) of the Sequence Listing; a substitute paper copy of the Sequence Listing, as well as an amendment directing its entry into the specification; and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). Applicants are required to comply with all of the requirements of 37 C.F.R. §§ 1.821 through 1.825. Any response to this Office Action which fails to meet all of these requirements will be considered non-responsive.

The disclosure is objected to because of the following informalities:

1) The description of the drawings beginning at page 16 should be identified by the heading --Brief Description of the Drawings--;

2) The specification does not comply with 37 CFR 1.821(d) requiring that nucleotide or amino acid sequences disclosed in the specification or drawings be identified by their assigned SEQ ID NOs. See for example, Figures 1 and 2, page 20, lines 9, 10, 22, 23, 28-30; page 21, line 9; page 24, lines28-30, 34-36; page 27, line 15; and page 32, line 1. With respect to sequences present in Fig. 1 and 2, the nucleotide and amino acid sequences may be identified by recitation of the assigned SEQ ID NOs in the description of the figures or in the figures themselves.

Appropriate correction is required.

Claim Objections

Claims 2-4, 9-12, 16-18, and 40 are objected to because of the following informalities:

Claims 2-4, 9-12, and 16-18 are dependent claims that refer to a previous claim by reciting "A", "An", "a" or "an" "... according to claim". In each claim "A", "An", "a" or "an" should be replaced with --the-- to put them in proper format for a dependent claim.

Claims 17 and 18 are directed in part to a non-elected invention, transgenic tissue or a transgenic multicellular organism. Claim 17 should be amended to be directed to a host cell, and claim 18 to a transgenic cell.

Claim 18 is dependent upon non-elected claim 6, and should be re-written in independent form. The following is suggested:

-- A transgenic cell comprising the nucleic acid molecule of claim 1, which expresses human Akt-3 protein. --

In response to the restriction requirement of 1/24/05, claims 17, 18, and 40 have been identified in the claim listing filed 3/28/05 as being withdrawn. Each of these claims were included, at least in part, in elected group I. If Applicant wishes these claims withdrawn from future consideration, they should be cancelled in accordance with 37 CFR 1.121. Otherwise they should be identified as original or currently amended, as appropriate under 37 CFR 1.121, in a listing of the claims in response to this Office action.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4 rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. In the interest of compact prosecution, and in anticipation of SEQ ID NO: 2 being corrected, claim 4 has been included in this rejection.

The claimed nucleic acid embraces genomic DNA and mRNA found at least in the human from which the cloned sequences described in the specification were obtained, and likely other humans as well. Consequently, these claims read products of nature, which are non-statutory subject matter. The rejection would be overcome by limiting claim 1 to an --isolated nucleic acid--.

Claims 12 and 16 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility or a well established utility.

Claim 12 is directed to a nucleic acid molecule encoding SEQ ID NO: 3 (human Akt-3 protein, hAkt-3) "for use as a medicament", and claim 16 is directed to a "pharmaceutical composition" comprising the nucleic acid molecule encoding SEQ ID NO: 3 (human Akt-3 protein). In both cases the claims are directed to products for use specifically in treatment, presumably of some disease or condition. However, the specification does not contain an assertion of what the medicament or pharmaceutical composition would be used to treat. Nor is there any evidence of record for a well-established use of the recited nucleic acid in treatment of any disease or condition at the time the initial application was filed (12/22/98). Applicant is

reminded that the utility requirement must be met when the application is filed, and that utility must be based upon uses disclosed in the specification, not uses identified later. See *In re Kirk*, 153 USPQ 48 (CCPA 1967) at pages 52-53.

The only assertion of utility of any disclosed nucleic acid as a medicament (or pharmaceutical composition) is for treatment of cancer (page 9, lines 4-8). However, the specification preceding this assertion describes a number of different nucleic acid molecules having different functional characteristics, e.g. a nucleic acid molecule encoding hAkt-3, an antisense nucleic acid, probes and primers. The assertion on page 9 does not indicate which of the different nucleic acid molecules are to be used for treating cancer. This ambiguity is resolved at page 10, lines 8-10, where it is antisense constructs to Akt-3 that are taught for use in treating cancer, i.e. treatment of cancer involves inhibiting expression of Akt-3. At best, treatment of cancer with hAkt-3 coding sequence would do nothing, e.g. where the coding sequence is not operably linked to nucleic acid sequences required for its transcription and translation At worst, it may promote the cancer, assuming that increasing Akt-3 levels would do so. When the specification is taken as a whole, it does not teach using a nucleic acid molecule encoding hAkt-3 as a medicament or pharmaceutical for treating cancer.

Claims 12 and 16 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention for its recited intended uses.

This rejection would be overcome by deleting "for use as a medicament" from claim 12 (although this would be a duplicate of claim 1), and by deleting "pharmaceutical" from claim 16, line 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 40 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 40 is directed to a method for making a pharmaceutical formulation for the treatment of diseases associated with human Akt-3 protein expression. The method comprises the steps of contacting a host cell that expresses human Akt-3 protein with candidate compounds, selecting a compound, presumably one that is identified as binding hAkt-3 expressed by the cell, manufacturing bulk quantities of the selected compound and formulating it with a pharmaceutically acceptable carrier. The basis for the method is the presumption that a compound that binds hAkt-3 would have therapeutic value in treating an unspecified "disease associated with human Akt-3 protein expression."

The specification itself does not describe the method of claim 40, i.e. the claim itself is the sole guidance for practicing the method. Thus, the specification does not teach whether there are any specific requirements for the materials used to practice the method or how one would carry out this method. No particular type of cell is required, i.e. it could be a bacterium, a yeast or other fungal cell, a plant cell, or an animal cell. The specification describes bacterial and mammalian cells that express hAkt-3. The hAkt-3 expressed need not be functional. If functional, the cell is not required to provide other components of any of the pathways in which the hAkt-3 protein is or may be a part. Indeed, the specification mentions only a few such components of such pathways. The expression of hAkt-3 need not confer any phenotype upon the cell. The only requirement for the cell is that the cell express hAkt-3.

In order to identify a compound for incorporation into the pharmaceutical formulation, one would need to detect binding between the compound and the Akt-3 expressed in the cell, whether it is active or not. Akt-3 protein is an intracellular protein, so one would have to be able to detect such binding between the compound and hAkt-3 inside a cell. The specification provides no guidance as to how such binding would be detected. The specification provides no working examples of the claimed method, i.e. no experimental evidence that the method as claimed could in fact be used to identify compounds that bound to hAkt-3, much less the intended pharmaceutical compounds.

Since all that is required is binding, the presumption is that mere binding of the compound to hAkt-3 in a patient would be of therapeutic benefit for treating some unspecified disease or condition. Binding of the compound to hAkt-3 may produce one of three possible outcomes on the activity or functioning of hAkt-3 *in vivo*. It may have no effect, it may activate

or increase the activity of hAkt-3, or it may inhibit the activity of hAkt-3. The method, as claimed, would not distinguish between these three possibilities.

It is doubtful that a compound that binds to hAkt-3 without affecting its activity would be useful for therapy. The second and third possible effects, increasing or decreasing hAkt-3 activity, would be not be expected to be useful for treating the same diseases or conditions. Thus, compounds identified by the method may have no use, or mutually exclusive uses, depending upon whether hAkt-3 activity is to be stimulated or inhibited. However, the method does not include steps that would allow one to distinguish between these three possibilities, i.e. the method as recited is not capable of giving the result set forth in the preamble and the specification does not disclose additional steps that would do so.

The specification does not unequivocally teach a disease or condition that could be treated with a compound identified by this method. The specification (page 35, lines 14-17; page 36, lines 6-9) provides speculation that hAkt-3 is involved in cell survival, since it is activated by IGF-1, and that it "potentially may suppress apoptosis in tumor cells," and that "Akt-3 may prove to be an important target for the development of novel therapeutics for the treatment of cancer". If so, the specification provides no evidence that hAkt-3 is required for suppression of apoptosis in tumor cells, or that an inhibitor of hAkt-3 would overcome such suppression or be useful in treating cancer. As noted in the specification on page 35, one concern over the use of inhibitors of Akt proteins for treating cancer is the role they play in insulin signaling, and whether such inhibitors may induce diabetes. The results of Walker et al. (Biochem. J. 331: 299-308, 1998) suggest that Akt-3 may not be involved in insulin signaling in the major insulin-responsive tissues, or at least not as involved as Akt-1 and Akt-2. However, it expression in

brain, and proposed role in cell survival suggests the possibility that its inhibition might have deleterious consequences on survival of cells in the brain, such as neurons.

The disclosure of Walker suggests that the different Akt proteins may be of different consequence or importance in cancer. Walker (page 299, col. 1) discloses that some ovarian and pancreatic cancers overexpress PKBβ (Akt-2), while some breast cancers overexpress PKBα (Akt-1). Walker proposes identifying inhibitors that are selective for Akt-2 as potential drugs for treating ovarian and pancreatic cancers, not cancer in general. There is no evidence of record that Akt-3 is overexpressed in tumor cells, and the specification does not disclose any particular type of cancer that could be treated by a selective inhibitor of Akt-3.

The specification does not identify any disease that could be treated by a compound whose binding to Akt-3 would either have no effect on its activity or would increase its activity.

Therefore, in view of the near total lack of guidance on how to practice the claimed method, e.g. to detect binding between a test compound and hAkt-3 in the cells; the lack of steps in the claimed method to distinguish between compounds useless for treatment or potentially useful for mutually exclusive diseases or conditions; the failure to unequivocally identify diseases that the various identified compounds would be used to treat; the speculative, and therefore unpredictable, relationship between hAkt-3 activity and cancer; and the lack of any experimental demonstration that the method could in fact be used to identify compounds that bind to hAkt-3, much less that would be useful for treating a disease, it would clearly require excessive and undue experimentation to remedy these deficiencies and then practice the claimed invention.

Claims 1, 2, 9-12, 16-18 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (and its dependent claims) recite "encoding human Akt-3 protein or a functional equivalent, derivative or bioprecursor thereof, comprising the amino acid sequence illustrated in SEQ ID No. 3". Claim 18 also recites this language through its dependence from non-elected claim 6. It is unclear if or how recitation of "or a functional equivalent, derivative or bioprecursor thereof" limits the claims beyond the scope of "human Akt-3 protein ... comprising the amino acid sequence illustrated in SEQ ID No. 3". If the nucleic acid encodes SEQ ID NO: 3, which is disclosed as the amino acid sequence of human Akt-3 protein, it is unclear what the "functional equivalent, derivative or bioprecursor thereof" refer to. The terms functional equivalent, derivative, and bioprecursor are ambiguous. Without a precise definition of the functions possessed by a human Akt-3 protein or the properties of a derivative or bioprecursor one cannot determine the scope embraced by these terms. With respect to derivative, it is noted that peptides and amino acids produced by hydrolysis of the protein would be derivatives, as would the products of completely oxidizing (burning) the protein.

It is suggested that "or a functional equivalent, derivative or bioprecursor thereof," be deleted from claim 1, and not recited in claim 18 when put into independent form in response the objection of claim 18 above, which includes a suggested amended claim 18.

Claim 40 recites the limitation "a compound identified in step a) which binds to human Akt-3 protein" in step (b). There is insufficient antecedent basis for this limitation in the claim.

Step (a) does not direct the identification of any compound, among the plurality of candidate compounds brought into contact with the cell that binds hAkt-3.

Claims 1-4, 9-11, 17 and 18 would be allowable if rewritten as suggested above to overcome the objections and rejection(s) under 35 U.S.C. 101 and 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe, Ph.D. whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott D. Priebe

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